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PTO/SB/81 (10-00)

Approved for use through 10/31/2002. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

**REVOCATION AND SUBSTITUTE
POWER OF ATTORNEY OR
AUTHORIZATION OF AGENT**

| | |
|------------------------|-------------------------|
| Application Number | See Attached Appendix A |
| Filing Date | See Attached Appendix A |
| First Named Inventor | See Attached Appendix A |
| Group Art Unit | Not yet known |
| Examiner Name | Not yet known |
| Attorney Docket Number | See Attached Appendix A |

I hereby revoke all previous powers of attorney or authorizations of agent given in the above-identified application, and I hereby appoint:



Practitioner(s) named below:

Herb Boswell, Reg. No. 27,311; Laurel S. Bernstein, Reg. No. 37,280; Robert S. Andrews, Reg. No. 44,508; Neil Bartfeld Reg. No. 39,901; Matthew Grumpling, Reg. No. 44,427; Donna T. Ward, Reg. No. 48,271; Kenneth Tarbet, Reg. No. 43,181; Laura Handley, Reg. No. 39,704; Michael Shuster, Reg. No. 41,310; Susan T. Hubl, Reg. No. 47,668.

as my/our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith.

Please change the correspondence address to, and associate the above-identified application with:

0035807



Practitioners at Customer Number

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| | | | |
|--|-------|-----|--|
| <input type="checkbox"/> Firm or Individual Name | | | |
| Address | | | |
| Address | | | |
| City | State | Zip | |
| Country | | | |
| Telephone | Fax | | |

I am the:



Applicant/Inventor.



Assignee of record of 100% interest. See 37 CFR 3.71.

Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

SIGNATURE of Applicant or Assignee of Record

| | |
|-----------|--------------------------|
| Name | B. Lynne Parshall |
| Title | Executive Vice President |
| Signature | |
| Date | 4/21/03 |

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representatives (s) are required. Submit multiple forms if more than one signature is required, see below*.

*Total of 1 forms are submitted.

23546/01000/SF/5097417.1

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PATENT & TRADEMARK OFFICE
MAY 12 2003

Dkt. No.: See Attached Appendix A

Certificate Under 37 CFR § 3.73(b)

Applicant:

Application No.:

Filing Date:

Name of Assignee:

Type of Assignee (e.g. corporation, partnership, university, government agency, etc.):

See Attached Appendix A

See Attached Appendix A

See Attached Appendix A

Isis Pharmaceuticals, Inc.

Corporation

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The above-mentioned Assignee certifies that it is the assignee of the entire right, title and interest in the patent application identified above by virtue of either:

A. An assignment from the inventor(s) of the patent application identified above. The assignment was recorded in the Patent and Trademark Office at Reel _____, Frame _____. See attached Appendix A for information. OR

B. A chain of title from the inventor(s), of the patent application identified above, to the current assignee as shown below:

1. From: _____
To: _____
The document was recorded in the Patent and Trademark Office at
Reel: _____ and Frame: _____, or for which a copy thereof is attached.
2. From: _____
To: _____
The document was recorded in the Patent and Trademark Office at
Reel: _____ and Frame: _____, or for which a copy thereof is attached.
3. From: _____
To: _____
The document was recorded in the Patent and Trademark Office at
Reel: _____ and Frame: _____, or for which a copy thereof is attached.

Additional documents in the chain of title are listed on a supplemental sheet.

Copies of assignments or other documents in the chain of title are attached.

The undersigned has reviewed all the documents in the chain of title of the patent application identified above and, to the best of undersigned's knowledge and belief, title is in the assignee identified above.

The undersigned (whose title is supplied below) is empowered to sign this certificate on behalf of the assignee.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

4/21/03

Date

Signature

B. Lynne Parshall

Name

Executive Vice President and CFO

Title



APPENDIX A

Assignee: ISIS PHARMACEUTICALS, INC.

| ISI/S No. | Utility Docket No. | Application No. Filing Date: | Assignors | Group Art Unit | Reel | Frame | Recorded |
|--|--------------------|---------------------------------|-------------------------------------|-------------------|--------|-------|----------|
| HTS-0002 | 23546-07658 | 10/187,110 06/29/2002 | Donna T. Ward Kenneth W. Dobie | 1653 | 013076 | 0173 | 06/29/02 |
| Title: Antisense Modulation of ADAM12 Expression | | | | | | | |
| HTS-0010 | 23546-07659 | 10/178,258 06/20/2002 | Kenneth W. Dobie | 1645 | 013041 | 0242 | 06/20/02 |
| Title: Antisense Modulation of Heme Oxygenase 1 Expression | | | | | | | |
| HTS-0013 | 23546-07660 | 10/211,859 07/31/2002 | Brett P. Monia Kenneth W. Dobie | 1653 | 013172 | 0152 | 07/31/02 |
| Title: Antisense Modulation of Ran GTPase Activating Protein 1 Expression | | | | | | | |
| HTS-0020 | 23546-07661 | 10/161,983 05/31/2002 | Donna T. Ward Susan M. Freier | 1635 | 012975 | 0748 | 05/31/02 |
| Title: Antisense Modulation of Rb2/p130 Expression | | | | | | | |
| RTS-0213 | 23546-07663 | 10/154,708 05/22/2002 | Andrew T. Watt Susan M. Freier | 1645 | 012953 | 0176 | 05/22/02 |
| Title: Antisense Modulation of CDC-like Kinase 1 Expression | | | | | | | |
| RTS-0266 | 23546-07664 | 09/960,143 09/24/2001 | Brenda F. Baker Susan M. Freier | 1635 | 012201 | 0106 | 09/24/01 |
| Title: Antisense Modulation of Interleukin 8 Expression | | | | | | | |
| RTS-0297 | 23546-07666 | 09/920,671 08/01/2001 | C. Frank Bennett Susan M. Freier | 1635 | 012053 | 0521 | 08/01/01 |
| Title: Antisense Modulation of CoREST Expression | | | | | | | |



Assignee: ISIS PHARMACEUTICALS INC.



APPENDIX A
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Revised: May 8 2003

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APPENDIX A

Assignee: ISIS PHARMACEUTICALS, INC.

| ISI No. | Atty Docket No. | Application No. | Assignors | Group Art Unit | Reel | Frame | Recorded |
|--|-----------------|--------------------------|--------------------------------------|----------------|--------|-------|----------|
| RTS-0369 | 23546-07713 | 10/174,020 06/17/2002 | Brett P. Monia Kenneth W. Dobie | 1646 | 013023 | 0086 | 06/17/02 |
| Title: Antisense Modulation of Hypothetical Tumor Endothelial Marker Expression | | | | | | | |
| RTS-0374 | 23546-07714 | 10/174,456 07/17/2002 | Brett P. Monia Susan M. Freier | 1642 | 013034 | 0593 | 06/17/02 |
| Title: Antisense Modulation of G Protein-Coupled Receptor 49 Expression | | | | | | | |
| RTS-0375 | 23546-07715 | 10/100,100 07/18/2002 | Lex M. Cowser Kenneth W. Dobie | 1645 | 013131 | 0001 | 07/18/02 |
| Title: Antisense Modulation of LAM Domain Kinase 1 Expression | | | | | | | |
| RTS-0377 | 23546-07716 | 10/185,035 06/28/2002 | Brett P. Monia Kenneth W. Dobie | 1635 | 013076 | 0088 | 06/28/02 |
| Title: Antisense Modulation of DEXRAS1 Expression | | | | | | | |
| RTS-0379 | 23546-07717 | 10/187,659 07/01/2002 | Kenneth W. Dobie | 1642 | 013087 | 0188 | 07/01/02 |
| Title: Antisense Modulation of P2X4 Expression | | | | | | | |
| RTS-0333 | 23546-07724 | 10/008/789 11/08/2001 | C. Frank Bennett Kenneth W. Dobie | 1635 | 021370 | 0920 | 11/08/01 |
| Title: Antisense Modulation of Thyroid Hormone Receptor Interactor 6 Expression | | | | | | | |
| HTS-0026 | 23546-07755 | 10/293,998 11/11/2002 | Ming-Yi Chuang Kenneth W. Dobie | 1653 | 013504 | 0558 | 11/11/02 |
| Title: Modulation of B Protein-Coupled Receptor Re2 Expression | | | | | | | |

23546/01000/SF750947582

Revised: May 8, 2003